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EAN, EXAMINER	
ART UNIT	PAPER NUMBER
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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-28 are pending in the application.
   Of the above, claims 11, 21-28 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-10, 12-20 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-10, 12-20, drawn to compounds, compositions and method of using, classified in Classes 544,546,548,514 subclasses various .

II. Claim 11, drawn to a group of intermediates, classified in Classes 544, 546, 514,548, subclasses various .

III. Claims 21-24, drawn to another group of intermediates, classified in Class 544, subclasses various.

IV. Claims 25-26, drawn to a process of preparing a group of compounds, classified in Class 560, subclasses various.

V. Claims 27-28, drawn to a process of preparing a group of compounds, classified in Class 560, subclasses various.

Inventions I,II and III are related as mutually exclusive species in intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful to make other than the final product (M.P.E.P. § 806.04(b), 3rd paragraph), and the species are patentably distinct (M.P.E.P. § 806.04(h)).

In the instant case, the intermediate product is deemed to be useful as drugs and the inventions are deemed patentably distinct since there is nothing on this record to show them to be obvious variants. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit

evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

Groups I,II,IV and V are not related to each other.

If group I is elected, further restriction is required since group I contains a number of independent and patentably distinct inventions:

1.R_1 is

A. thiazolyl, oxazolyl mono-substituted by a non-heterocyclic group.

B. isoxazolyl, isothiazolyl mono-substituted by a non-heterocyclic group.

C. thiazolyl, oxazolyl mono-substituted by a heterocyclic group. Each heterocyclic represents an independent and distinct invention.

D. isoxazolyl, isothiazolyl mono-substituted by a heterocyclic group. Each hetrocyclic represents an independenct and distinct invention.

2. R_7 is

A. thiazolyl, oxazolyl

B. isothiazolyl, isoxazolyl

3. R_4 is

A. phenyl

B. thiazoyl, oxazolyl

4. R_{4a} is

A. phenyl

B. thiazoyl, oxazolyl

The compounds of group 1A2A3A4A are distinct from other groups. Group 1A2A3A4A would not be a reference under 35 USC 103 against the compounds of additional hetero ring containing group. Further, note that the heterocyclic moieties cannot be considered as conventional substituents, but rather form a new core of the molecule each time that they are present. Since no common core is present, the inventions are misjoined.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 USC 103 of the other invention.

During a telephone conversation with Mr. Crowley on July 19,1994 a provisional election was made without traverse to prosecute the invention of group I1A2A3A4A, the species of claim

8, claims 8,9,and the subject matter of claims 1-7, 10, 12-20 wherein R_1,R_7, R_4,R_{4a} are as defined in group 1A2A3A4A. Affirmation of this election must be made by applicant in responding to this Office action. Claims 11, 21-28 and the subject matter of claims 1-7,10, 12-20 besides group 1A2A3A4A are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Claims 1-7,10,12-20 are rejected as being drawn to improper markush groups. The deletion of the non-elected subjected matter would overcome the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure how to use the invention.

The following reasons apply:

1. Applicants' disclosure constitutes an invention to experiment, that is, the disclosure "present enormous work-loads that would require undue experimentation to find proper operative

chemical synthesis, reaction conditions, therapeutic mode of administration, dosage the like.

Further, with respect to the prima facie case of non-enablement, it is noted that a single embodiment may provide broad enablement is cases involving predictable factors, such as mechanical (In re Myers) or electrical elements. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more is required. In re Fisher 427 F.2d 833, 166 USPQ 18 (CCPA 1970). Here, applicants' fail to provide those having ordinary skill in the art reasonable assurance, as by adequate representative examples, that myriad of compounds falling within the scope of the claims can be prepared and used. See In re Surrey, 370 F.2d 349, 151 USPQ 724 (CCPA 1966).

2. The data set forth in the specification relate to in vitro studies of the claimed compounds with respect to their inhibitory effect on specified enzymes. There are no in vivo studies and there is no data in the record which correlates in vitro studies with in vivo utilization and usefulness. There is nothing in the record which establishes that the claimed protease inhibitors are effective to treat AIDS in humans.

3. Enzyme inhibitory effect is very structural, steric, configurational and sequence specific. It is very much like lock and key situation. Applicants fails to provide objective

evidence to substantiate the myriads of compounds are useful for the alleged utility. Note Zeffren reference and Wade reference.

4. In vitro assay is not sufficient since aids encompasses a variety of degenerative diseases of the CNS . Additional efficacy in a behavioral assay is required in order to confirm that the compounds were being absorbed, were crossing the blood-brain barrier, and were actually exerting an effect on the central nervous system. Note Shutske et al reference.

Claims 1-7, 12-20 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-7,12-20 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms " cycloalkyl", "alkyl" "alkoxy" and terms which contain "alkyl", "alkoxy" are beyond the enablement since there is no carbon number limitation.

The proviso statement in claims 1-2 is not understand.

6K Claims 1-10,12-20 are provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims of copending application Serial No.07/998,114 and SN 08/185,666 .

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims1-10,12-20 are provisionally rejected under 35 U.S.C. § 102(e) as being anticipated by copending application Serial No. 08/185,666 and SN 07/998,114.

Copending application Serial No. 07/998,114 and SN 08/185,666 has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. § 102(e) if patented. This provisional rejection under 35 U.S.C. § 102(e) is based upon a presumption of future patenting of the conflicting copending application.

This provisional rejection under section 102(e) might be overcome either by a showing under 37 C.F.R. § 1.132 that any unclaimed invention disclosed in the copending application was derived from the inventor of this application and is thus not the invention "by another", or by a showing of a date of invention of any unclaimed subject matter prior to the effective U.S. filing date of the copending application under 37 C.F.R. § 1.131.

In view of the papers filed April 25, 1994, it has been found that this application, as filed, through error and without any deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 C.F.R. § 1.48. The inventorship of this application has been changed by adding Arthur J. Cooper as a joint inventor.

Applicants' PTO-1449 and the accompany references are noted with appreciation. The references have been placed in the file.

Applicants' fax is noted with appreciation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JANE whose telephone number is (703) 308-4705.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

JTF JULY 19, 1994

J. T. Fan

JANE T. FAN
PRIMARY EXAMINER
ART UNIT 123